REMARKS

A Replacement Abstract is attached following page 65 of this response and is believed to be compliant with all applicable rules and regulations.

The rejection of claims 20-23 under 35 U.S.C. § 112 as indefinite is respectfully traversed. Claims 20-23 are amended to replace the term "medicament" with "pharmaceutical formulation." Support for this change may be found in the specification, for instance, at least in the paragraph bridging pages 1 and 2 which recites "pharmaceutical preparations" near the end. The last line of claim 20 requires the presence of a pharmaceutically acceptable carrier. Thus, it is clear that claims 20-23 are directed to a composition and the carrier is required. Claims 21-23 depend from claim 20 and include all of the limitations thereof. Accordingly, these claims are definite and reconsideration and withdrawal of the rejection is respectfully requested.

The objection to claim 42 is respectfully traversed. Claim 42 is amended to reflect that it is directed to a pharmaceutical composition comprising at least one compound corresponding to structure (I A), (I B) or (II) of claim 1. Thus, claim 42 is amended to make more clear that it is dependent from claim 1 and includes the limitations thereof. There are significant elements in claim 1 that are not present in claim 20, see, for instance, the last several lines of claim 1. As stated in § 706.03(k), differences in scope between claims are enough to make two otherwise similar claims allowable. Claims 20 and 42 are not identical and are sufficiently different in scope that both of them should be allowed. Reconsideration and withdrawal of the objection is respectfully requested.

The rejection of claims 36-39 under 35 U.S.C. § 112 as indefinite is respectfully traversed.

Persons of skill in the art are familiar with the medical conditions or illnesses that are affected by modulating nucleoside transport proteins, adenosine kinase, adenosine deaminase or A1, A2 or A3 receptors. These receptors play a crucial role in physiological and pathophysiological processes which are known to persons of skill in the art. Accordingly, any medical conditions or illnesses known to be affected by modulating nucleoside transport

proteins, adenosine kinase, adenosine deaminase or A1, A2 or A3 receptors should fall within the scope of the present claims.

The relevant question is whether one of skill in the art could understand the scope of the claim. The MPEP states that:

> In reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent. See, e.g., Solomon v. Kimberly-Clark Corp., 216 F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000).

In the present case, that test is met, because one of skill in the art would readily understand that the claims requires administering a claimed compound to modulate nucleoside transport proteins, adenosine kinase, adenosine deaminase or A1, A2 or A3 receptors. Therefore, one of skill in the art could readily determine whether or not some activity constitutes infringement of these claims.

Reconsideration and withdrawal of this rejection are respectfully requested.

The rejections of claims 28-31 and 36-40 under 35 U.S.C. § 112, first paragraph, for lack of enablement, are respectfully traversed. For purposes of clarity, the following remarks are offered not only in response to the rejection of claims 28-31, but also the separate rejections of claims 36-39 and claim 40.

The enablement requirement is satisfied where the specification describes the claimed subject matter in such a way as to enable any person skilled in the art to which it pertains to make and/or use the invention. Thus, enablement is judged in view of the combined teachings of the specification and the knowledge of one skilled in the art.

The U.S. Court of Customs and Patent Appeals has stated that "[t]he first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance." *In re*

Marzocchi, 169 USPQ 367 , 369 (CCPA 1971). The court also added that "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." *In re Marzocchi*, 169 USPQ 367 , 370 (CCPA 1971).

The present record includes no such statement or other explanation as to why the truth of the accuracy of statements in the disclosure should be doubted.

All of the medical conditions and illnesses mentioned in claim 28 were linked to the MK801 binding site of the NMDA channels in the prior art. Consequently, among those skilled in the art it can be reasonably expected that a compound that acts as a ligand on such a receptor may have a beneficial effect on one or more of the given medical conditions and illnesses. Thus, the action on a receptor is usually considered sufficient proof that a given class of active substances is useful in the treatment of a disease related to said receptor.

As support for the link between the in vitro assay directed to the inhibition of the specific binding of the ligand MK801 and the claimed disease states, see, for example; US 6,399,574 131 and the references cited therein as well as US 6,071,966 131. In each case corresponding applications were before the priority date of the present application.

The disclosure in US 6,071,966 131 teaches that compounds that inhibit MK801 binding (see table 7) are useful in the treatment of a number of different diseases (column 36) which are currently encompassed by claim 28 of the present application.

Additionally, it is generally accepted among those skilled in the art that compounds which bind to the ionotropic NMDA receptor as determined in the assay of the present application, i.e., compounds that inhibit MK801 binding, are NMDA antagonists. NMDA agonists would not be active in this assay. It is also generally accepted among persons of skill in the art that *in vitro* test results provide a good indicator *in vivo* action. The United States Patent and Trademark Office has not routinely required evidence of *in vivo* activity to

confer patentability. Further, as explained above, the patent laws, as interpreted by the Federal Circuit require only objective enablement.

The tested compounds are representative of the compounds of general formulae IA, IB and II, i. e. they are representative of various chemical, steric and electronic factors influencing the overall properties of the resulting compounds. Accordingly, the tested compounds are sufficient to demonstrate the general usefulness of the compounds as claimed.

The statement in the Office Action that the NMDA receptor antagonists CNS 5161 and GV 150526, which are structurally different from the compounds of general formulae IA, IB and II, had not shown clinical efficacy is respectfully traversed. The references of Lees et al. and Walters et al. merely disclose that formal efficacy studies in man are considered justified. As formal efficacy studies for CNS 5161 and GV 150526 are considered worthwhile according to Lees et al. and Walters et al. these references add further support to the fact that compounds which are effective as NMDA receptor antagonists in *in vitro* assays also have clinical efficacy in the treatment of cerebral ischemias and cerebral oedemas.

Moreover, although the Low et al. reference discloses that compounds acting as NMDA receptor antagonists need to be analyzed for neurotoxicity, the reference does not describe any neurotoxicity for the presently claimed compounds. Quite the contrary is true, since it is explicitly stated that it is not known whether such compounds are neurotoxic in humans.

It is common knowledge among those skilled in the art that any pharmaceutically active compound may also exhibit adverse effects. However, this does not say anything about the compound's clinical usefulness, since in many cases the adverse effects can be avoided by choosing the right dosage or through combined administration with other substances. Accordingly, the present disclosure credibly establishes that the inventively claimed compounds act as NMDA antagonists and that that they can be reasonably expected to be clinically useful in the treatment of the recited diseases.

Thus, the specification as filed (i) specifically identifies the claimed compounds, (ii) provides a method of synthesizing these compounds and (iii) provides at least one use for the

claimed compounds. As indicated above, the burden is on the Patent Office to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. On the present record there is no such explanation, and no apparent reason is offered to support the notion that the statements in the specification are not true or accurate.

As a result, the claims are properly enabled, and reconsideration and withdrawal of the rejection are respectfully requested.

The rejection of claims 28-31 and 36-40 under 35 U.S.C. 112, first paragraph, for lack of enablement, is respectfully traversed. These claims have been amended to delete the words "prophylaxis" and "prevent" in accordance with the Examiner's kind suggestions. Accordingly, the claims are directed to methods of treating and are properly enabled. Reconsideration and withdrawal of this rejection are respectfully requested.

The rejection of claims 1-7 and 9-40 under 35 U.S.C. 112, first paragraph, for lack of enablement in allegedly not enabling making solvates and hydrates, is respectfully traversed.

The law relating to enablement, which clarifies that only objective enablement is required, is explained above.

Persons skilled in the art would reasonably expect that many of the claimed compounds may form solvates (including hydrates). In particular, compounds with hydroxy and carboxy substituents are likely to form hydrates through the formation of hydrogen bonds.

Moreover, persons skilled in the art are also familiar with methods for the generation of solvates, which can be seen, from standard textbooks or journals, for example, from pages 202-208 of the literature publication in Drugs. Pharm. Sci. 1999, Volume 95.

Consequently, once a person of skill in the art has knowledge of the claimed compounds, those skilled in the art can apply routine methods of synthesis to determine whether a specific compound forms solvates and - if so - what type of solvates. Accordingly,

the claims directed to the solvates and hydrates of the claimed compounds should also be allowable. Reconsideration and withdrawal of this rejection are respectfully requested.

CONCLUSION

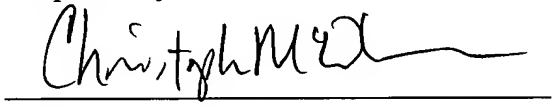
In view of the foregoing, the application is respectfully submitted to be in condition for allowance, and prompt favorable action thereon is earnestly solicited.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #029310.52760US).

Respectfully submitted,

August 2, 2005



J. D. Evans
Registration No. 26,269
Christopher T. McWhinney
Registration No. 42,875

CROWELL & MORING LLP
Intellectual Property Group
P.O. Box 14300
Washington, DC 20044-4300
Telephone No.: (202) 624-2500
Facsimile No.: (202) 628-8844
JDE:CTM:tlm (389125)